REMARKS

Claims 9 and 11-21 are pending in the present application.

The rejection of Claims 9 and 11-22 under 35 U.S.C. §103(a) over Ishioka et al (Am J Ophthalmol. 1994 Dec 15;118(6):723-9) in view of Stuchlik et al (WO 99/34830) and Nussenblatt (Int. Rev. Immunol. 1997, Vol. 14, No. 1, pp. 67-79) is traversed.

The present invention provides, in part, a method for treating retinopathy, comprising administering to a subject in need thereof an effective amount of an agent comprising a tricyclo compound of formula (I) or a pharmaceutically acceptable salt thereof. (Claim 9)

In contrast, Ishioka et al disclose the clinical effects of the immunosuppressive agent FK506 in patients with noninfectious uveitis. Applicants note, however, that uveitis is not the same as or related to retinopathy. Uveitis is an inflammatory condition of the uvea, which includes that iris, ciliary body, and chorioidea. However, the uvea does not include the retina (see enclosed definition of the uvea). In Ishioka et al, it is disclosed that patients suffering from sympathetic ophthalmia, which is a form of uveitis, showed improvement following administration of FK506, but patients suffering from retinal vasculitis did not (see page 723, left column, lines 9-6 from the bottom).

At no point does Ishioka et al disclose or suggest that a compound within the scope of the present claims is effective for the treatment of retinopathy.

The Examiner cites Stuchlik et al for teaching lipophilic immunosuppressive agents that are obtained by dissolving or dispersing an immunosuppressant in a physiologically acceptable base containing an excipient to enhance permeation of drugs into ophthalmic tissue. Therefore, the disclosure of Stuchlik et al relates to enhancing the permeability of an immunosuppressant through the cornea. However, Stuchlik et al do not compensate for the

deficiencies in the disclosure of Ishioka et al. Specifically, Stuchlik et al fail to disclose or suggest a tricyclo compound of formula (I) or a pharmaceutically acceptable salt thereof for treating retinopathy.

In recognition of the deficiency in the combined disclosures of Ishioka et al and Stuchlik et al, the Examiner asserts that Nussenblatt provides motivation to administer a macrolide as an ocular anti-inflammatory and, thus, treat retinopathy. However, Applicants note that Nussenblatt relates to *uveitis* in Behcet's Disease patients. Behcet's Disease is a complicated disorder with a significant number of manifestations and sequelae, which are manifest in any number or combinations both acute and chronic. Even as highlighted by Nussenblatt, the ocular effects of Behcet's Disease may be *exclusively associated with anterior uveitis* in some patients and, thus, unrelated to retinopathy (see, e.g., the paragraph bridging pages 67-68 and the last paragraph on page 68 of Nussenblatt). Complications, such as retinal and optic atrophy, are only disclosed as *potential* complications (see, e.g., Abstract). Therefore, although Nussenblatt relates to ocular complications of the Behcet's Disease and treatment thereof, this reference does not provide specific motivation to administer a compound of formula (I) to a patient with a *recognized need* to treat retinopathy.

The U.S. Courts have recently held that a method of administering a compound "to a human in need thereof" is properly construed to require that the compound be administered to human with a recognized need to treat the recited disorder (*Jansen v. Rexall Sundown Inc.*, **copy enclosed herewith**). As in *Jansen*, the claims of the present invention are drawn to administering a compound of formula (I) "to a subject in need" of treating retinopathy. Therefore, there must be a specific disclosure or suggestion in the cited prior art of a subject with a recognized need to treat retinopathy. Therefore, the failure of the combined disclosures of Ishioka et al, Stuchlik et al, and Nussenblatt to disclose or suggest

administering a compound of formula (I) "to a subject in need" of treating retinopathy would make the present invention unobvious in view thereof.

Moreover, MPEP §2142 states: "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation... to modify the reference... Second, there must be a reasonable expectation of success. Finally, the prior art reference... must teach or suggest all the claim limitations." Even if the artisan were to combine the disclosures of Ishioka et al, Stuchlik et al, and Nussenblatt the only expected advantage could be for treatment of uveitis. Therefore, the combined disclosures of Ishioka et al, Stuchlik et al, and Nussenblatt would fail to render the present invention obvious as the combined disclosure fail to provide the requisite "reasonable expectation of success" for treatment of retinopathy.

In view of the foregoing, Applicants submit that the present invention is not obvious in view of the combined disclosures of Ishioka et al, Stuchlik et al, and Nussenblatt. Accordingly, Applicants request withdrawal of this ground of rejection.

The rejection of Claim 22 under 35 U.S.C. §102(a) over Stuchlik et al (WO 99/34830) is obviated by amendment.

Claim 22 has been canceled in response to the outstanding Office Action. Therefore, this ground of rejection is believed to be moot. Withdrawal of this rejection is requested.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

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Jansen
v.
Rexall Sundown Inc.

U.S. Court of Appeals Federal Circuit

No. 03-1069

Decided September 8, 2003

PATENTS
[1] Patent construction -- Prosecution history estoppel (§ 125.09)
Patent construction -- Claims -- Broad or narrow (§ 125.1303)
Claims for method of "treating or preventing" pernicious anemia by administering folic acid and vitamin B12 "to a human in need thereof" are properly construed to require that compound be administered to human with recognized need to treat or prevent anemia, since "treating or preventing" phrase in preambles sets forth objective of claimed method, and body of claim directs that method be performed on subject "in need," and since prosecution history supports this construction, in that patentability hinged upon addition of phrases to claim language, and phrases were added simultaneously, and should be read together; thus, claimed method is not practiced if claimed vitamins in claimed doses are administered for some purpose other than treating pernicious anemia.
[2] Infringement -- Construction of claims (§ 120.03)
Infringement -- Literal infringement (§ 120.05)
Federal district court properly granted summary judgment that administration of defendant's over-the-counter dietary supplement does not infringe claimed method of "treating or preventing" pernicious anemia by administering folic acid and vitamin B12 "to a human in need thereof," even though amounts of folic acid and vitamin B12 in accused supplement are within ranges claimed in patent, since asserted claims are properly construed to require that compound be administered to human with recognized need to treat or prevent anemia, since, without evidence that accused product is prescribed by medical doctors, plaintiff has shown no more than theoretical possibility that defendant's customers take accused product knowingly to treat pernicious anemia, and since such "metaphysical doubt" is insufficient to raise genuine issue of material fact.

PATENTS
Particular patents -- Chemical -- Vitamins
4,945,083, Jansen, safe oral folic-acid-containing vitamin preparation, summary judgment of noninfringement affirmed.

Appeal from the U.S. District Court for the Southern District of Indiana, Tinder, J.

Action by Christian J. Jansen Jr. against Rexall Sundown Inc. for contributory patent infringement and inducement. Plaintiff appeals from summary judgment of noninfringement. Affirmed.

John C. McNett and Steve E. Zlatos, of Woodard, Emhardt, Naughton, Moriarty & McNett, Indianapolis, Ind., for plaintiff-appellant.

Gary H. Levin and Lynn B. Morreale, of Woodcock Washburn, Philadelphia, Pa., for defendant-appellee.

Before Lourie, Rader, and Schall, circuit judges.

Lourie, J.

Christian J. Jansen, Jr., appeals from the final decision of the United States District Court for the Southern District of Indiana granting summary judgment that Rexall Sundown, Inc. has not infringed Jansen's U.S. Patent 4,945,083. Jansen v. Rexall Sundown, Inc. , No. IP 00-1495-C-T/G (S.D. Ind. Sept. 25, 2002). Because the court correctly construed the patent claims and correctly found no genuine issues of material fact on the question of infringement, we affirm.

BACKGROUND

Jansen is the sole inventor and owner of the '083 patent, which is directed to methods of "treating or preventing macrocytic-megaloblastic anemia" by administering a combination of folic acid and vitamin B12 "to a human in need thereof." '083 patent, col. 6, ll. 20-24, ll. 37-41. According to the patent,

deficiencies of either folic acid or vitamin B12 can cause macrocytic- megaloblastic anemia, also referred to as pernicious anemia, while a deficiency of vitamin B12 can also cause neurological problems. Id. at col. 4, ll. 13- 25. When folic acid alone is utilized to treat macrocytic-megaloblastic anemia, the folic acid may mask a vitamin B12 deficiency. Id.; *see also* id. at col. 3, l. 65 - col. 4, l. 5. An objective of Jansen's invention is to administer both supplements together to avoid the masking problem. Id. at col. 4, ll. 25-48. The independent claims read as follows:

1. A method of *treating or preventing macrocytic-megaloblastic anemia* in humans which anemia is caused by either folic acid deficiency or by vitamin B12 deficiency which comprises administering a daily oral dosage of a vitamin preparation *to a human in need thereof* comprising at least about 0.5 mg. of vitamin B12 and at least about 0.5 mg. of folic acid.

4. A method of *treating or preventing macrocytic-magaloblastic [sic] anemia* in humans which anemia is caused by either folic acid deficiency or by vitamin B12 deficiency which comprises orally administering combined vitamin B12 and folic acid *to a human in need thereof* in sufficient amounts to achieve an oral administration of at least about 0.5 mg. of vitamin B12 and at least about 0.5 mg. of folic acid within one day. Id. at col. 6, ll. 20-24, ll. 37-41 (emphases added).

The '083 patent is a seventh-generation continuation of a patent application filed in 1970. Every member of the '083 patent's lineage was abandoned in favor of the succeeding application until the '083 patent issued in 1990. Jansen's first application claimed the method as follows:

A method of treating or preventing anemia in humans which comprises administering a daily oral dosage of a vitamin preparation containing at least .5 mg. of vitamin B12 and at least .5 mg. of folic acid, whereby anemia can safely be treated orally without determining whether it is caused by folic ***1156** acid deficiency or by vitamin B12 deficiency. *In re Jansen*, 187 USPQ 743, 744 (CCPA 1975). That original claim, while specifying approximately the same amounts of folic acid and vitamin B12, does not specify the type of anemia being treated and says nothing about any need on the part of the human subject. The U.S. Patent and Trademark Office ("PTO") found that claim, as well as claims directed to the composition of matter, to be obvious in light of prior art that taught administration of folic acid alone in the claimed range, vitamin B12alone in the claimed range, and combinations of the two in smaller doses than claimed. The PTO found unpersuasive Jansen's argument that administration of both components in the higher, claimed doses was an unexpected solution to the masking problem, and the Court of Customs and Patent Appeals affirmed the PTO's rejections. Id. at 746. In his next five applications, Jansen persistently attempted to gain allowance of his claims in slightly different form, yet the PTO consistently rejected his attempts. In the prosecution of his seventh application, Jansen repeated his masking-avoidance argument and submitted an article that asserted that the medical community had come to realize the effectiveness of folic acid-vitamin B12 combination therapy to treat pernicious anemia only after Jansen's invention date. *See* William H. Crosby, *Improvisation Revisited--Oral Cyanocobalamin Without Intrinsic Factor for Pernicious Anemia*, 140 Arch. Intern. Med. 1582 (1980). The examiner agreed but noted that the claims, being directed to unspecified anemia, were not commensurate in scope with Jansen's showing of unexpected results. Jansen thereafter agreed to cancel his composition of matter claims and to narrow his method claims by requiring a specific type of anemia, *viz.*, macrocytic-megaloblastic anemia, rather than anemia generally, and by adding to the claims the phrase "to a human in need thereof." The PTO then issued the '083 patent to Jansen.

Rexall markets to the general public an over-the-counter dietary supplement presently known as Folic Acid XTRATM that contains folic acid and vitamin B12 within the claimed ranges. The Rexall product is labeled and advertised for maintenance of proper blood homocysteine levels, but not for prevention or treatment of macrocytic-megaloblastic anemia.

Jansen sued Rexall for inducement of and contributory infringement of the '083 patent. In the district court Jansen argued that all people are "human[s] in need" of "treat[ment] or prevent[ion] of macrocytic-megaloblastic anemia," but the court, without definitively construing the "in need" phrase, rejected that argument. *Jansen*, slip op. at 14. Citing, *inter alia*, Rapoport v. Dement , 254 F.3d 1053 [59 USPQ2d 1215] (Fed. Cir. 2001), the court then construed the phrase "treating or preventing macrocytic-megaloblastic anemia" to require that, in order to infringe the patent, the human subject of the claimed method take the compound with the intent of treating or preventing macrocytic-megaloblastic anemia. *Jansen*, slip op. at 16. Because the court found no evidence of such intent or purpose on the

part of Rexall's customers, the court granted summary judgment of noninfringement. *Id.* at 16-17.

Jansen timely appealed to this court, and we have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

Summary judgment is appropriate if "there is no genuine issue as to any material fact and . . . the moving party is entitled to a judgment as a matter of law." Fed. R. Civ. P. 56(c). "The evidence of the nonmovant is to be believed, and all justifiable inferences are to be drawn in his favor." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 255 (1986). We review a district court's grant of a motion for summary judgment *de novo*. Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp., 149 F.3d 1309, 1315 [47 USPQ2d 1272] (Fed. Cir. 1998).

A determination of patent infringement requires a two-step analysis. "First, the court determines the scope and meaning of the patent claims asserted . . . [Second,] the properly construed claims are compared to the allegedly infringing device." Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1454 [46 USPQ2d 1169] (Fed. Cir. 1998) (en banc) (citations omitted). Step one, claim construction, is an issue of law, Markman v. Westview Instruments, Inc., 52 F.3d 967, 970-71 [34 USPQ2d 1321] (Fed. Cir. 1995) (en banc), *aff'd*, ***1157**517 U.S. 370 [38 USPQ2d 1461] (1996), that we review *de novo*, *Cybor*, 138 F.3d at 1456. Step two, comparison of the claim to the accused device, requires a determination that every claim limitation or its equivalent is found in the accused device. Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 29 [41 USPQ2d 1865] (1997). Those determinations are questions of fact. Bai v. L & L Wings, Inc., 160 F.3d 1350, 1353 [48 USPQ2d 1674] (Fed. Cir. 1998).

On appeal, Jansen first argues that the court improperly construed the claims. More specifically, he contends that the court's construction improperly added to the claims an intent element, which is contrary to law as well as contrary to the ordinary meaning of the claim language, which does not suggest that the infringer's state of mind is relevant. Nor does the '083 patent's prosecution history, according to Jansen, suggest that the infringer's state of mind is relevant. He also argues that *Rapoport* does not support the court's view that a direct infringer must purposefully perform the claimed method, and that in any event *Rapoport* is distinguishable because that case, unlike this case, did not involve a claim to a method of prevention of a disease. According to Jansen, the phrase "a human in need thereof" encompasses a person who does not know that his or her serum levels of folic acid and vitamin B12 are adequate. Jansen secondly argues that he presented sufficient evidence of infringement to avoid summary judgment. According to Jansen, Rexall's formulation and labeling are circumstantial evidence of direct infringement by Rexall's customers.

Rexall responds that the court's claim construction does not add an intent element to the claims except as required by the particular language of the claims themselves. Rexall also contends that, just as in *Rapoport*, the claims in the '083 patent should be interpreted to require that the target group ("human[s] in need thereof") practice the method for the stated purpose ("treating or preventing macrocytic-megaloblastic anemia"), especially where, as here, the prosecution history reveals that both limitations were added for patentability. According to Rexall, a "human in need thereof" is someone either suffering from macrocytic-megaloblastic anemia or at a recognized risk, such as by medical diagnosis, of developing that condition. Rexall also responds that there is no evidence that it markets its product to the target group for the claimed purpose; on the contrary, it contends that it markets its product only for regulation of blood homocysteine levels. Rexall further contends that, even if there were some evidence of direct infringement by its customers, it is not liable for indirect infringement, for it has not intended to cause infringement and there are substantial noninfringing uses of its product, thereby negating inducement of and contributory infringement.

We begin our claim construction, as always, with the ordinary meaning of the claim language. Rexnord Corp. v. Laitram Corp., 274 F.3d 1336, 1341 [60 USPQ2d 1851] (Fed. Cir. 2001). That language requires that the method be performed on "a human in need thereof" and that the method be used "for treating or preventing macrocytic-megaloblastic anemia." The parties do not dispute what "macrocytic-megaloblastic anemia" means; instead, they dispute how the "treating or preventing" phrase and the "to a human in need thereof" phrase should be read. The issue reduces to whether such a human must know that he is in need of either treatment or prevention of that condition.

A similar issue arose in *Rapoport*, an interference

proceeding before the PTO's Board of Patent Appeals and Interferences. The count in that case read as follows:

A method *for treatment of sleep apneas* comprising administration of a therapeutically effective amount of a Formula I azapirone compound or a pharmaceutically effective acid addition salt thereof *to a patient in need of such treatment* . . . .

254 F.3d at 1056 (emphases added). On appeal we gave weight to the ordinary meaning of the preamble phrase "for treatment of sleep apneas," interpreting it to refer to sleep apnea, *per se*, not just "symptoms associated with sleep apnea." *Id.* at 1059. Rapoport argued that the count was unpatentable on the ground that a prior art reference disclosed that a form of the compound recited in the claim could be administered, not for treatment of sleep apnea itself, but for treatment of anxiety and breathing difficulty, a symptom of apnea. *Id.* at 1061. We rejected that argument, stating, "There is no disclosure in the [prior art reference that the compound] is administered to patients suffering from sleep apnea *with the intent to cure the underlying condition*." *Id.* (emphasis added). Thus, the claim was interpreted to require that the method be practiced ***1158** with the intent to achieve the objective stated in the preamble.

[1] Just as in *Rapoport*, it is natural to interpret the nearly parallel language in the '083 patent claims in the same way. In both *Rapoport* and this case, the claim preamble sets forth the objective of the method, and the body of the claim directs that the method be performed on someone "in need." In both cases, the claims' recitation of a patient or a human "in need" gives life and meaning to the preambles' statement of purpose. *See* Kropa v. Robie , 187 F.2d 150, 152 [88 USPQ 478] (CCPA 1951) (stating the rule that a preamble is treated as a limitation if it gives "life and meaning" to the claim). The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed. We need not decide whether we would reach the same conclusion if either of the "treating or preventing" phrase or the "to a human in need thereof" phrase was not a part of the claim; together, however, they compel the claim construction arrived at by both the district court and this court.

Our conclusion as to the meaning of the claims is bolstered by an analysis of the prosecution history. The prosecution history is often useful to ascertain the meaning of the claim language. Indeed, claims are not construed in a vacuum, but rather in the context of the intrinsic evidence, *viz.*, the other claims, the specification, and the prosecution history. *See* DeMarini Sports, Inc. v. Worth, Inc. , 239 F.3d 1314, 1327 [57 USPQ2d 1889] (Fed. Cir. 2001). In this case, the "treating or preventing macrocytic-megaloblastic anemia" phrase and the "to a human in need thereof" phrase were added to gain allowance of the claims after almost twenty years of repeatedly unsuccessful attempts to gain allowance of claims without those phrases. We must therefore give them weight, for the patentability of the claims hinged upon their presence in the claim language. *See* Smith v. Magic City Kennel Club, Inc. , 282 U.S. 784, 790 (1931) ("The applicant[,] having limited his claim by amendment and accepted a patent, brings himself within the rules that if the claim to a combination be restricted to specified elements, all must be regarded as material, and that limitations imposed by the inventor, especially such as were introduced into an application after it had been persistently rejected, must be strictly construed against the inventor and looked upon as disclaimers."). Furthermore, because both phrases were added simultaneously to overcome the same rejection, they should be read together, meaning that the word "thereof" in the phrase "to a human in need thereof" should be construed to refer to the treatment or prevention of macrocytic-megaloblastic anemia. Finally, that "need" must be recognized and appreciated, for otherwise the added phrases do not carry the meaning that the circumstances of their addition suggest that they carry. In other words, administering the claimed vitamins in the claimed doses for some purpose other than treating or preventing macrocytic- megaloblastic anemia is not practicing the claimed method, because Jansen limited his claims to treatment or prevention of that particular condition in those who need such treatment or prevention. Thus, the '083 patent claims are properly interpreted to mean that the combination of folic acid and vitamin B12 must be administered to a human with a recognized need to treat or prevent macrocytic-megaloblastic anemia.

[2] Given that claim construction, we turn to the issue whether Jansen has raised a genuine issue of material fact regarding infringement. We conclude that he has not. Jansen has asserted indirect infringement by Rexall, premised on direct infringement by Rexall's customers. *See* Met-Coil Sys. Corp. v. Korners Unlimited, Inc. , 803 F.2d 684, 687 [231 USPQ 474] (Fed. Cir. 1986) ("Absent direct infringement of the patent claims,

there can be neither contributory infringement nor inducement of infringement." (citations omitted)). Jansen's theory of infringement is primarily based upon his construction of the claim that those who do not affirmatively know that they do not need to take steps to prevent or treat macrocytic-megaloblastic anemia are still "in need thereof." As explained above, that claim construction is incorrect. Jansen nonetheless asserts that he has circumstantial evidence of direct infringement by Rexall's customers under the claim construction we and the district court have adopted. Specifically, he contends that Rexall's formulation, having folic acid and vitamin B12in such large quantities as his claims call for, as well as Rexall's labeling stating that "[i]t is especially important to take B-12 along with Folic acid because Folic ***1159** acid can mask a B-12 deficiency," are evidence that some customers do knowingly take the Rexall product to treat or prevent macrocytic-megaloblastic anemia.

While Jansen is correct that it is theoretically possible that some of Rexall's customers do take the Rexall product knowingly to treat or prevent macrocytic-megaloblastic anemia, and therefore directly infringe his patent, his evidence is quite weak. In fact, he has shown no more than a theoretical possibility or "metaphysical doubt," which is insufficient to create a *genuine* issue of material fact. *See* Anderson, 477 U.S. at 261 (citing Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 586 (1986)). The district court's decision that there were no genuine issues of material fact on the question of infringement was therefore correct.

Use of an over-the-counter product like Rexall's is quite different from the use of a product pursuant to a prescription from a medical doctor. In the latter case, a prescription is evidence of a diagnosis and a knowing need to use the product for the stated purpose. Jansen does not have evidence of that in this case. Rexall's product is provided with a label stating that the product can be used for maintenance of blood homocysteine levels, and purchasers do not necessarily know that they are in need of preventing or treating macrocytic-megaloblastic anemia. Instead, Jansen has only conjecture that some purchasers of the Rexall product might meet the claim requirements. The district court therefore did not err in holding that he failed to present sufficient proof of infringement to create a genuine issue of material fact and to thereby avoid summary judgment of noninfringement.

CONCLUSION

The district court correctly construed the claims of the '083 patent and properly determined that Jansen did not present sufficient evidence to create a genuine issue of material fact relating to infringement by Rexall. Accordingly, we

AFFIRM.

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